

REMARKS

By the above amendment, claims 1-12 and 18 are canceled and new claims 25-35 are added along with arguments to place this application in condition for allowance.

In review, new claim 25 corresponds generally to claim 1 and new claim 35 corresponds generally to claim 18. New claims 26 and 27 correspond to claims 2 and 3. New claims 28, 29, 33, and 34 correspond roughly to claim 9. New claim 30 corresponds generally to claim 10. New claim 31 corresponds generally to claim 11, and new claim 32 corresponds generally to claim 32.

First, Applicants object to the Examiner's failure to consider the prior art submitted in the IDS filed on February 7, 2006. The Examiner alleges that no translation was supplied with the three foreign references cited in the IDS. This allegation is not correct since an Abstract was cited with each of the references. For the Examiner's benefit, a copy of each abstract is attached herewith and an acknowledged PTO-1449 is requested.

The Wittmar poster is being re-filed to resolve the legibility issue with this reference.

Turning now to the office action, the Examiner has raised a number of objections against the claims from a definiteness standpoint. In response to these objections, the pending claims are canceled and replaced with new claims 25-35.

Concerning claim 1, this claim is rewritten taking into account original claims 19 and 21 and the practical embodiments 1 and 2. In this regard and according to the invention, the comb polymer may consist of three different building blocks: a polyol backbone on the one hand, and attached to that backbone, a hydrophobic side chain and a side chain carrying

an amino function on the other hand. Regarding the variables, which characterize the side chains, the scope of application is limited within certain ranges described in the original disclosure. In order to overcome the objections to claim 1, claim 25 includes reference to the free hydroxyl groups of the polyol backbone of the polymer. Since this number is not expressly listed, the variable n_{OH} is used. n_{OH} corresponds to the number of hydroxyl groups of the free polyol backbone, which means the number of hydroxyl groups before the attachment of the side chains. The practical embodiments 1.2 and 1.3 disclose the preparation of a comb polymer starting with a polyol backbone, in which the number of free hydroxyl functions n_{OH} is 300. Depending on the degree of the following functionalization with said side chains, a certain number of hydroxyl groups may remain unmodified. In order to define this number p_{OH} , i.e., the remainder of unmodified hydroxyl group, the number of hydroxyl groups of the comb polymer, is introduced to claim 1.

If the Examiner should have a problem with the language of claim 25 and this is the only problem preventing allowance of the application, the Examiner is requested to telephone the undersigned so that the problem can be worked out and the allowance of the application can be expedited.

The Examiner also expressed a problem with the zeta potential since this is a feature of the colloidal dispersion not the particle themselves. Since the Examiner is correct in this observation, "colloidal particles" is replaced with "colloidal solution of the particles" in new claim 25 and the appropriate dependent claims.

The limitations found in original claim 3 are now incorporated into claim 25 to allay the Examiner's concerns regarding the definition of the stabilizer.

Concerning the use of the trademark iloprost, this term has been replaced with its generic description so that the objection in this regard is no longer valid.

No new matter is introduced by new claims 28 and 29 since they are supported by the specification in page 6, lines 31 and 21 and page 7, lines 1-3.

Based on the revisions to claim 1 as now embodied in claim 25, and the other changes now incorporated into the new claims, the rejection based on 35 USC §112, second paragraph, is no longer appropriate and should be withdrawn.

Turning now to the prior art rejection, claim 1 was rejected under 35 USC §103 based on the combination of United States Patent No. 6,908,626 to Cooper et al. (D1) and the article authored by Kissel (D3) or these two references in combination with United States Patent No. 5,049,582 to Adler et al. (D2). The Examiner admits that D3 does not teach the limitation concerning CMC and relies on D1 to allege that the use of this in D3 is obvious. D2 is cited to address the limitation concerning iloprost.

Applicants submit that a prima facie case of obviousness does not exist when considering the changes to claim 1 via the submission of new independent claim 25.

D3 teaches nanoparticles comprising the comb polymers of the instant claims in combination with insulin. A combination of such a comb polymer with CMC as a part of a stabilizer is not disclosed so that D3 cannot be said to teach or suggest the invention.

In D1, the combination of nanoparticles and micronized particles are employed to produce a formulation that has immediate release and controlled release characteristics. CMC is used as a stabilizer for nanoparticles of hardly soluble active components. Thereby it is suggested, that the stabilization is linked with the suppression of agglomeration and

particle growth. The size of the nanoparticles is critical to obtain the immediate release functionality so that the stabilizer is used to avoid particle growth.

The Examiner's attention is directed to paragraph [0042] of Applicants' published patent application. Here it is disclosed that comb polymers do not build stable colloidal particles on their own, especially in aqueous solutions. Instead and under these types of conditions, the comb polymer would rather be present in dissolved form and do not demonstrate the desired particle formation. This is the problem which is addressed by the present invention and it is significantly different compared with the one described in D1.

In making the rejection, the Examiner overstates the extent of the teachings of D1 to support the modification of D3. The mere fact that CMC is used to stabilize the nanoparticles in a mixture of nanoparticles and micronized particles is insufficient to support the contention of obviousness. This is because the invention is concerned with colloidal particles and the problems associated with these particles in aqueous solutions. The invention and D1 are concerned with completely different systems and problems. Consequently, one of skill in the art knowing the teaching of D1 concerning stabilizing nanoparticles in a mix of nanoparticles and micronized particles, would not conclude that CMC could be used in the context of the present invention, which relates to the formation of colloidal particles. Put another way, the Examiner does not have the proper reasoning to apply the teachings of D1 to D3 and allege that claim 25 is obvious.

Moreover, a major advantage of colloidal particles according to the present invention is their unique and unexpected stability upon nebulization. This feature is particularly important regarding an inhalation of the colloidal particles. D1 does not give any hint disclosing this beneficial property. This unexpected benefit is a rebuttal of the allegation of

obviousness if the Examiner insists that D1 can be used to modify D3. These unexpected benefits are backed up with evidence in the specification showing the stability of the formulation upon nebulization. The Examiner's attention is directed to Figure 1(a-d) and the nebulization tests in paragraphs [0090-0094] of the published application. Here it is clear that the CMC-containing colloidal particles maintained their particle size distribution after nebulization, whereas the comparative formulation showed significant aggregation after nebulization, see Figure 1(d).

D2 teaches that iloprost is useful in treating or preventing kidney damage. However, according to the instant invention the benefit of the at least one active component does not only arise from its pharmaceutical activity, but also from the stabilization of the colloidal particles. This additional beneficial effect of certain active components is not disclosed by the teaching of D2. Thus, even if D2 were combined with D1 and D3, the deficiencies in the rejection based on D3 are not remedied and either a prima facie case of obviousness is not established or it is rebutted by the unexpected benefits associated with the invention.

To recap, the rejection based on D3 and D1 is improper since the Examiner does not have the proper reasoning to modify D3 with the teachings of D1. D2 does not remedy this problem and a prima facie case of obviousness does not exist. In addition, the invention produces unexpected benefits in terms of the colloidal particle stabilization in the context of nebulizing applications and these benefits rebut any contention of obviousness.

Since claim 25 is demonstrated to be patentable over the cited prior art, its dependent claims are also in condition for allowance.

Applicants also contend that since claim 25 is patentable, the restriction requirement should be withdrawn so that the method of use claims are allowed along with the product claims.

Accordingly, the Examiner is requested to examine this application in light of this response and pass all pending claims onto issuance.

If the Examiner believes that an interview would be helpful in expediting the allowance of this application, the Examiner is requested to telephone the undersigned at 202-835-1753.

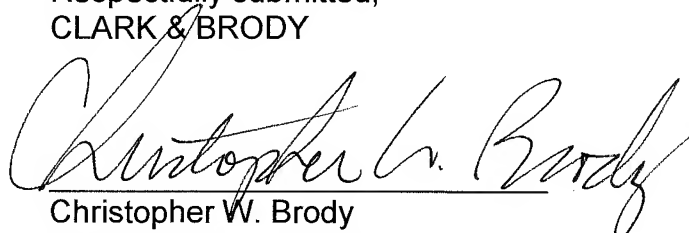
The above constitutes a complete response to all issues raised in the Office Action dated February 16, 2010.

Again, reconsideration and allowance of this application is respectfully requested.

Applicants petition for a one month extension of time.

Please charge the extension of time fee (\$65) and any fee deficiency or credit any overpayment to Deposit Account No. 50-1088.

Respectfully submitted,
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Docket No.: 12007-0051
Date: June 9, 2010

Association of active agent with colloidal polymer, preferably new polymeric branched polyol ester, useful for controlled transmucosal administration of e.g. peptide, DNA construct or vaccine

Patent number: DE19839515
Publication date: 2000-03-09
Inventor: KISSEL THOMAS (DE); BREITENBACH ARMIN (DE); JUNG TOBIAS (DE); KAMM WALTER (DE)
Applicant: KISSEL THOMAS (DE); BREITENBACH ARMIN (DE); JUNG TOBIAS (DE); KAMM WALTER (DE)
Classification:
- international: A61K9/51; A61K47/48; A61K9/51; A61K47/48; (IPC1-7): A61K9/14
- european: A61K9/51; A61K47/48W6B
Application number: DE19981039515 19980829
Priority number(s): DE19981039515 19980829

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Abstract of DE19839515






A pharmaceutical composition contains at least one colloidal polymer-active agent association (A). An independent claim is included for novel polymers (I) which are branched polyol esters consisting of a central molecule (II) to which short-chain, biodegradable hydroxycarboxylic acid ester groups (III) are attached. The reaction parameters (i.e. nature and amount of (II) and catalyst system, nature and length of (III), reaction temperature and reaction time) are selected to optimize (I) for use as the polymer component of (A).

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Microencapsulated biologically active substances that contain a water-soluble or water-dispersible comb polymer

Patent number: DE10104991
Publication date: 2002-08-08
Inventor: ZERRER RALF (DE); MORSCHHAEUSER ROMAN (DE)
Applicant: CLARIANT GMBH (DE)
Classification:
- international: **A01N25/28; B01F17/00; B01F17/54; B01J13/18; C08G63/688; C08G81/00; A01N25/26; B01F17/00; B01F17/54; B01J13/06; C08G63/00; C08G81/00;** (IPC1-7): C09D5/14; C08G63/668
- european: A01N25/28; B01F17/00M; B01F17/00V; B01F17/00Z; B01J13/18; C08G63/688; C08G81/00
Application number: DE20011004991 20010203
Priority number(s): DE20011004991 20010203

Also published as:

 WO02062856 (A3)
 WO02062856 (A2)
 EP1368387 (A3)
 EP1368387 (A2)
 US2004048749 (A1)

[more >>](#)[Report a data error here](#)**Abstract of DE10104991**






The invention relates to microencapsulated biologically active substances that contain a water-soluble or water-dispersible comb polymer, consisting of a main polymer chain and polyester side-groups that carry sulfonic acid groups and that are linked with the main polymer chain via ester groups.

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Colloidal nanoparticular carriers comprising loaded or non-loaded water soluble comb polymers and their use in mucosal applications

Patent number: EP1132416
Publication date: 2001-09-12
Inventor: KISSEL THOMAS PRF DR (DE); BREITENBACH ARMIN DR (DE); JUNG TOBIAS DR (DE); KAMM WALTER DR (DE)
Applicant: AVENTIS RES & TECH GMBH & CO (DE)
Classification:
- international: **A61K9/51; C08G85/00; A61K9/00; A61K9/51; C08G85/00; A61K9/00; (IPC1-7): C08G85/00; A61K9/14**
- european: A61K9/51; C08G85/00
Application number: EP20000104920 20000308
Priority number(s): EP20000104920 20000308

Cited documents:

 US5929196
 US5919442
 WO995256
 GB2145422
 DE1983951
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Abstract of EP1132416

The use of a colloidal nanoparticulate carrier (A) containing at least one water-soluble comb polymer (I) for mucosal application is claimed. An independent claim is also included for a colloidal nanoparticulate carrier (A') containing a backbone formed from water-soluble polyol(s) and hydrophobic side-chains, providing an amphiphilic character, and optionally ionic groups, where the backbone polymer has a weight average molecular weight (Mw) of 10000-30000 (preferably 15000-25000, especially 20000) and the side chains preferably have a combined Mw of 45000-100000 (especially 50000-80000, particularly 50000-60000).

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